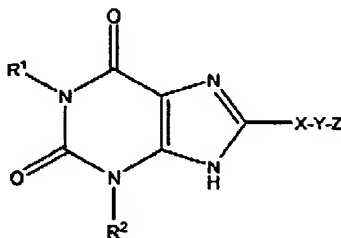


BEST AVAILABLE COPYResponse to December 5, 2005 Office Action
Serial No. 10/719,102
CVT No. 01-0163-CIP2**AMENDMENTS TO THE CLAIMS**

The following listing of claims will replace all prior versions and listing of claims in the application. For the Examiner's convenience a complete listing of all claims incorporating the amendments made herein is attached as Appendix A.

LISTING OF CLAIMS:

1. (Currently Amended) A process for the preparation of a compound of Formula I:



Formula I

wherein:

R¹ and R² are independently optionally substituted alkyl;

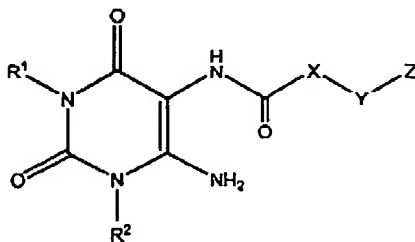
X is optionally substituted arylene or optionally substituted heteroarylene;

Y is a covalent bond or lower alkylene; and

Z is optionally substituted monocyclic aryl or optionally substituted monocyclic heteroaryl;

comprising;

cyclizing a compound of the formula (3):



(3)

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wherein R^1 , R^2 , X, Y, and Z are as defined above.

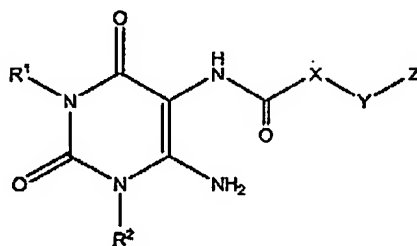
2. (Original) The process of claim 1, wherein the compound of formula (3) is cyclized in an inert solvent in the presence of a base.

3. (Original) The process of claim 2, wherein the inert solvent is methanol and the base is aqueous sodium hydroxide solution.

4. (Original) The process of claim 3, wherein R^1 and R^2 are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

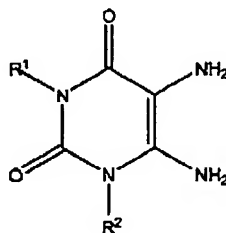
5. (Original) The process of claim 4, wherein R^1 is n-propyl, R^2 is ethyl, and Z is 3-trifluoromethylphenyl.

6. (Currently Amended) The process of claim 1, wherein the compound of formula (3):



(3)

is prepared by a method comprising contacting a compound of the formula (2);



(2)

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with a compound of the formula $Z-Y-X-CO_2H$ in the presence of a carbodiimide or with a compound of the formula $Z-Y-X-C(O)Hal$, where Hal is chloro or bromo.

7. (Currently Amended) The process of claim 6, wherein the compound of formula (3) is reacted with a compound of the formula $Z-Y-X-CO_2H$ in methanol ~~in the presence of a coupling agent used to form amide bonds.~~

8. (Currently Amended) The process of claim 7, wherein the carbodiimide coupling agent used to form amide bonds is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

9. (Currently Amended) The process of claim 6, wherein the compound of formula (3) is reacted with a compound of the formula $Z-Y-X-C(O)Cl$.

10. (Original) The process of claim 9, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.

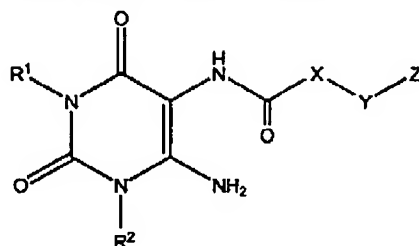
11. (Original) The process of claim 10, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.

12. (Original) The process of claim 6, wherein R^1 and R^2 are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

13. (Original) The process of claim 12, wherein R^1 is n-propyl, R^2 is ethyl, and Z is 3-trifluoromethylphenyl, namely 3-ethyl-1-propyl-8-{1-[(3-trifluoromethylphenyl)methyl]pyrazol-4-yl}-1,3,7-trihydropurine-2,6-dione.

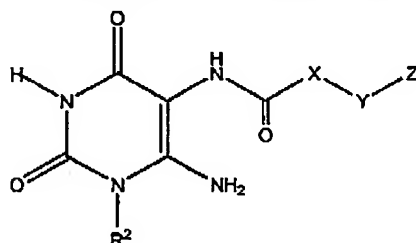
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14. (Original) The process of claim 1, wherein the compound of the formula:



(3)

is prepared by a method comprising contacting a compound of the formula;



(16)

with a compound of the formula R¹L, in which L is a leaving group.

15. (Original) The process of claim 14, wherein R¹ is lower alkyl optionally substituted by cycloalkyl, and L is iodo.

16. (Original) The process of claim 15, wherein the reaction is carried out in the presence of a base in an inert solvent.

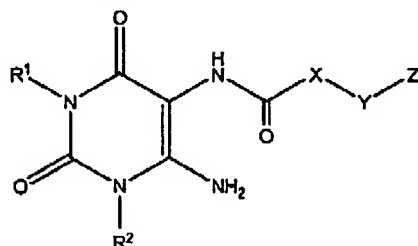
17. (Original) The process of claim 16, wherein the base is potassium carbonate and the inert solvent is N,N-dimethylformamide.

18. (Original) The process of claim 17, wherein R¹ and R² are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

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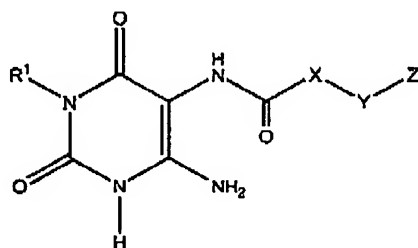
19. (Original) The process of claim 18, wherein R^1 is n-propyl, R^2 is ethyl, and Z is 3-trifluoromethylphenyl.

20. (Original) The process of claim 1, wherein the compound of the formula:



(3)

is prepared by a method comprising contacting a compound of the formula;



(13)

with a compound of the formula R^2L , in which L is a leaving group.

21. (Original) The process of claim 20, wherein R^2 is lower alkyl optionally substituted by cycloalkyl, and L is iodo.

22. (Original) The process of claim 21, wherein the reaction is carried out in the presence of a base in an inert solvent.

23. (Original) The process of claim 22, wherein the base is potassium carbonate and the inert solvent is N,N -dimethylformamide.

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28. (Currently Amended) The process of claim 27, wherein the coupling-agent used to form ~~amide bonds~~carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

29. (Currently Amended) The process of claim 26, wherein the compound of formula (15) is reacted with a compound of the formula Z-Y-X-C(O)Cl.

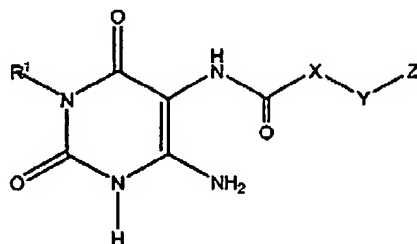
30. (Original) The process of claim 29, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.

31. (Original) The process of claim 30, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.

32. (Original) The process of claim 31, wherein R¹ and R² are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

33. (Original) The process of claim 32, wherein R¹ is n-propyl, R² is ethyl, and Z is 3-trifluoromethylphenyl.

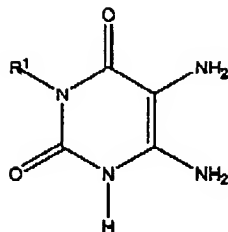
34. (Currently Amended) The process of claim 19, wherein the compound of the formula:



(13)

is prepared by a method comprising contacting a compound of the formula:

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(12)

with a compound of the formula $Z-Y-X-CO_2H$ in the presence of a carbodiimide or a compound of the formula $Z-Y-X-C(O)Hal$, where Hal is chloro or bromo.

35. (Currently Amended) The process of claim 34, wherein the compound of formula (12) is reacted with a compound of the formula $Z-Y-X-CO_2H$ in methanol in the presence of a coupling agent used to form amide bonds.

36. (Currently Amended) The process of claim 35, wherein the coupling agent used to form amide bonds carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

37. (Currently Amended) The process of claim 34, wherein the compound of formula (12) is reacted with a compound of the formula $Z-Y-X-C(O)Cl$.

38. (Original) The process of claim 37, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.

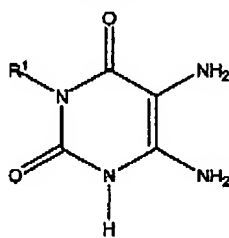
39. (Original) The process of claim 38, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.

40. (Original) The process of claim 39, wherein R^1 and R^2 are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

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41. (Original) The process of claim 40, wherein R^1 is n-propyl, R^2 is ethyl, and Z is 3-trifluoromethylphenyl.

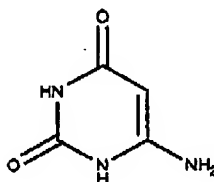
42. (Original) The process of claim 34, wherein the compound of the formula:



(12)

is prepared by a method comprising the steps of:

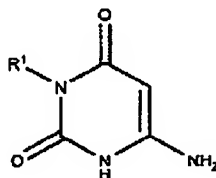
a) contacting a compound of the formula:



with hexamethyldisilazane in the presence of an acid catalyst;

b) contacting the product thus formed with R^1L , where L is a leaving group, followed by;

c) contacting the product thus formed:

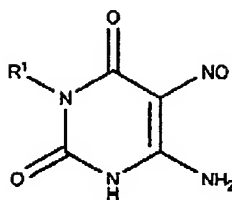


(10)

with a mixture of sodium nitrite in acetic acid/water; and

d) contacting the product thus formed:

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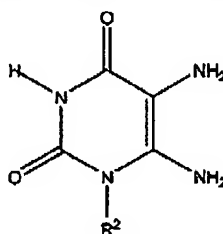


(11)

with a mixture of aqueous ammonia and sodium dithionite.

43. (Original) The process of claim 42, wherein in step a) R^1 is lower alkyl, L is iodo, and the acid catalyst is ammonium sulfate.

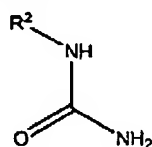
44. (Original) The process of claim 26, wherein the compound of the formula:



(15)

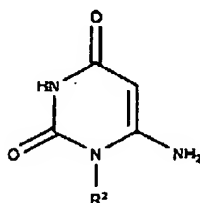
is prepared by a method comprising the steps of:

a) contacting a compound of the formula:



with ethyl cyanoacetate in the presence of a base in a protic solvent;

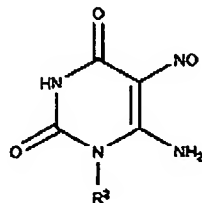
b) contacting the product thus formed:



with a mixture of sodium nitrite in acetic acid/water, and

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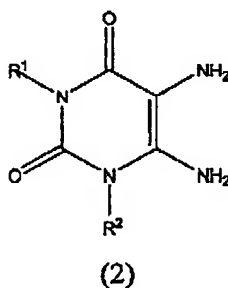
- c) contacting the product thus formed:



with a mixture of aqueous ammonia and sodium dithionite.

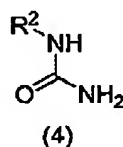
45. (Original) The process of claim 44, wherein the base is sodium ethoxide and the protic solvent is ethanol.

46. (Original) The process of claim 6, wherein the compound of formula:



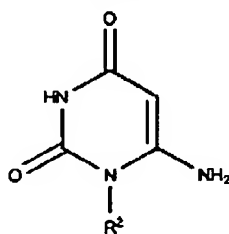
is prepared by a method comprising the steps of:

- a) contacting a compound of the formula:



with ethyl cyanoacetate in the presence of a base in a protic solvent;

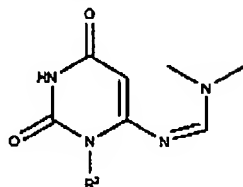
- b) contacting the product thus formed:



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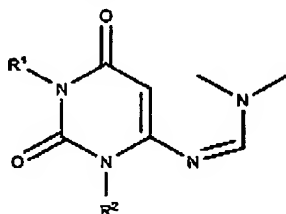
with the dimethylacetal of N,N-dimethylformamide;

c) contacting the product thus formed:



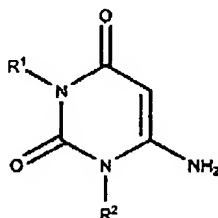
with a compound of formula R¹L, in which L is a leaving group;

d) contacting the product thus formed:



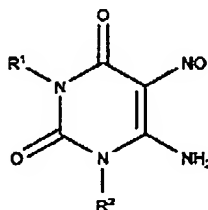
with aqueous ammonia;

e) contacting the product thus formed:



with a mixture of sodium nitrite in acetic acid/water; and

f) contacting the product thus formed:



with a mixture of aqueous ammonia and sodium dithionite.

47. (Original) The process of claim 46, wherein the base is sodium ethoxide and the protic solvent is ethanol.

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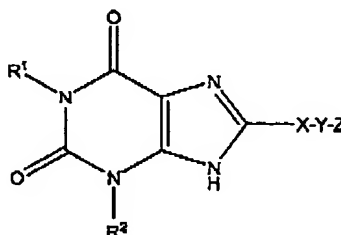
Claims 48-55 Cancelled

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APPENDIX B

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1. A process for the preparation of a compound of Formula I:



Formula I

wherein:

R^1 and R^2 are independently optionally substituted alkyl;

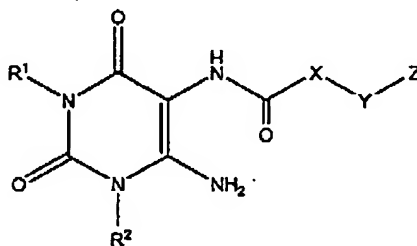
X is optionally substituted heteroarylene;

Y is a covalent bond or lower alkylene; and

Z is optionally substituted monocyclic aryl or optionally substituted monocyclic heteroaryl;

comprising;

cyclizing a compound of the formula (3):



(3)

wherein R^1 , R^2 , X, Y, and Z are as defined above.

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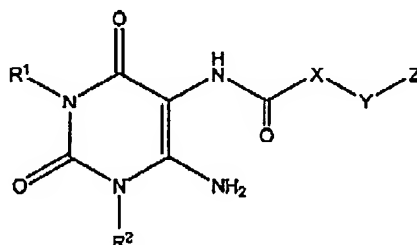
2. The process of claim 1, wherein the compound of formula (3) is cyclized in an inert solvent in the presence of a base.

3. The process of claim 2, wherein the inert solvent is methanol and the base is aqueous sodium hydroxide solution.

4. The process of claim 3, wherein R^1 and R^2 are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

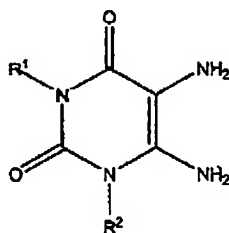
5. The process of claim 4, wherein R^1 is n-propyl, R^2 is ethyl, and Z is 3-trifluoromethylphenyl.

6. The process of claim 1, wherein the compound of formula (3):



(3)

is prepared by a method comprising contacting a compound of the formula (2);



(2)

with a compound of the formula $Z-Y-X-CO_2H$ in the presence of a carbodiimide or with a compound of the formula $Z-Y-X-C(O)Hal$, where Hal is chloro or bromo.

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7. The process of claim 6, wherein the compound of formula (3) is reacted with a compound of the formula $Z-Y-X-CO_2H$ in methanol.

8. The process of claim 7, wherein the carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

9. The process of claim 6, wherein the compound of formula (3) is reacted with a compound of the formula $Z-Y-X-C(O)Cl$.

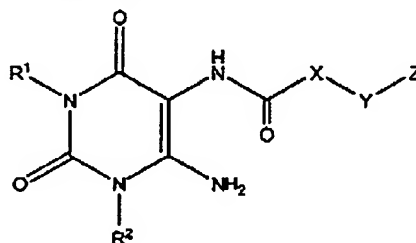
10. The process of claim 9, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.

11. The process of claim 10, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.

12. The process of claim 6, wherein R^1 and R^2 are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

13. The process of claim 12, wherein R^1 is n-propyl, R^2 is ethyl, and Z is 3-trifluoromethylphenyl, namely 3-ethyl-1-propyl-8-{1-[(3-trifluoromethylphenyl)methyl]pyrazol-4-yl}-1,3,7-trihydropurine-2,6-dione.

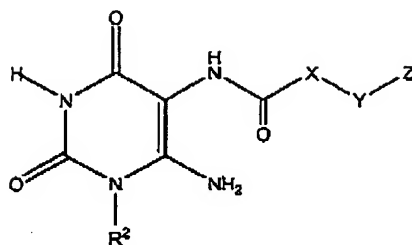
14. The process of claim 1, wherein the compound of the formula:



(3)

is prepared by a method comprising contacting a compound of the formula;

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(16)

with a compound of the formula R¹L, in which L is a leaving group.

15. The process of claim 14, wherein R¹ is lower alkyl optionally substituted by cycloalkyl, and L is iodo.

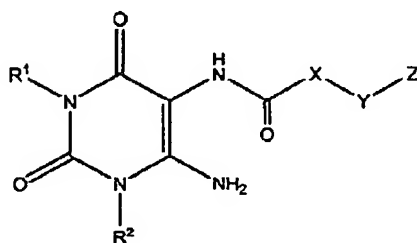
16. The process of claim 15, wherein the reaction is carried out in the presence of a base in an inert solvent.

17. The process of claim 16, wherein the base is potassium carbonate and the inert solvent is N,N-dimethylformamide.

18. The process of claim 17, wherein R¹ and R² are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

19. The process of claim 18, wherein R¹ is n-propyl, R² is ethyl, and Z is 3-trifluoromethylphenyl.

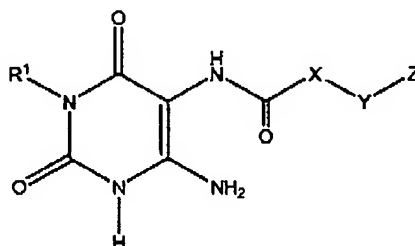
20. The process of claim 1, wherein the compound of the formula:



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(3)

is prepared by a method comprising contacting a compound of the formula;



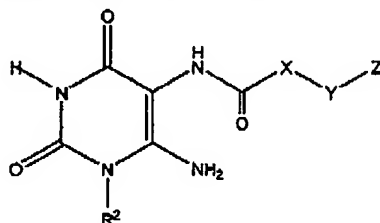
(13)

with a compound of the formula R²L, in which L is a leaving group.

21. The process of claim 20, wherein R² is lower alkyl optionally substituted by cycloalkyl, and L is iodo.
22. The process of claim 21, wherein the reaction is carried out in the presence of a base in an inert solvent.
23. The process of claim 22, wherein the base is potassium carbonate and the inert solvent is N,N-dimethylformamide.
24. The process of claim 23, wherein R¹ and R² are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.
25. The process of claim 24, wherein R¹ is n-propyl, R² is ethyl, and Z is 3-trifluoromethylphenyl.

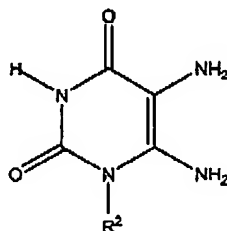
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26. The process of claim 14, wherein the compound of the formula:



(16)

is prepared by a method comprising contacting a compound of the formula:



(15)

with a compound of the formula $Z-Y-X-CO_2H$ in the presence of a carbodiimide or with a compound of the formula $Z-Y-X-C(O)Hal$, where Hal is chloro or bromo.

27. The process of claim 26, wherein the compound of formula (15) is reacted with a compound of the formula $Z-Y-X-CO_2H$ in methanol.

28. The process of claim 27, wherein the carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.

29. The process of claim 26, wherein the compound of formula (15) is reacted with a compound of the formula $Z-Y-X-C(O)Cl$.

30. The process of claim 29, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.

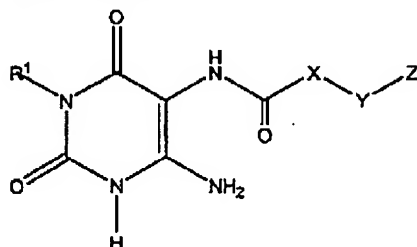
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31. The process of claim 30, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.

32. The process of claim 31, wherein R^1 and R^2 are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.

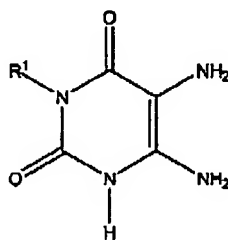
33. The process of claim 32, wherein R^1 is n-propyl, R^2 is ethyl, and Z is 3-trifluoromethylphenyl.

34. The process of claim 19, wherein the compound of the formula:



(13)

is prepared by a method comprising contacting a compound of the formula:



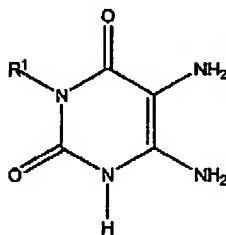
(12)

with a compound of the formula $Z-Y-X-CO_2H$ in the presence of a carbodiimide or a compound of the formula $Z-Y-X-C(O)Hal$, where Hal is chloro or bromo.

35. The process of claim 34, wherein the compound of formula (12) is reacted with a compound of the formula $Z-Y-X-CO_2H$ in methanol.

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36. The process of claim 35, wherein the carbodiimide is 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide.
37. The process of claim 34, wherein the compound of formula (12) is reacted with a compound of the formula Z-Y-X-C(O)Cl.
38. The process of claim 37, wherein the reaction is carried out in an inert solvent in the presence of a tertiary base.
39. The process of claim 38, wherein the inert solvent is acetonitrile and the tertiary base is triethylamine.
40. The process of claim 39, wherein R¹ and R² are independently lower alkyl, X is pyrazol-4-yl, Y is methylene, and Z is optionally substituted phenyl.
41. The process of claim 40, wherein R¹ is n-propyl, R² is ethyl, and Z is 3-trifluoromethylphenyl.
42. The process of claim 34, wherein the compound of the formula:

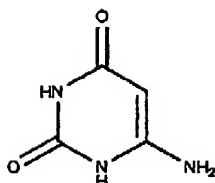


(12)

is prepared by a method comprising the steps of:

- a) contacting a compound of the formula:

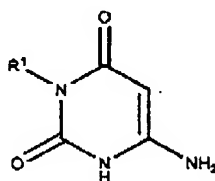
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with hexamethyldisilazane in the presence of an acid catalyst;

b) contacting the product thus formed with R^1L , where L is a leaving group, followed by;

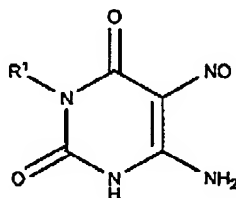
c) contacting the product thus formed:



(10)

with a mixture of sodium nitrite in acetic acid/water; and

d) contacting the product thus formed:



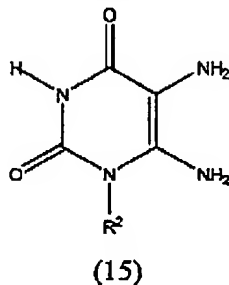
(11)

with a mixture of aqueous ammonia and sodium dithionite.

43. The process of claim 42, wherein in step a) R^1 is lower alkyl, L is iodo, and the acid catalyst is ammonium sulfate.

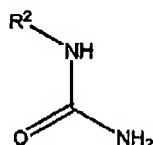
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44. The process of claim 26, wherein the compound of the formula:



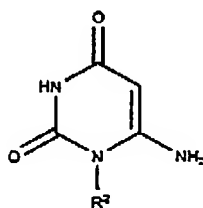
is prepared by a method comprising the steps of:

- a) contacting a compound of the formula:



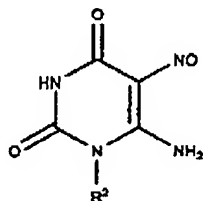
with ethyl cyanoacetate in the presence of a base in a protic solvent;

- b) contacting the product thus formed:



with a mixture of sodium nitrite in acetic acid/water; and

- c) contacting the product thus formed:

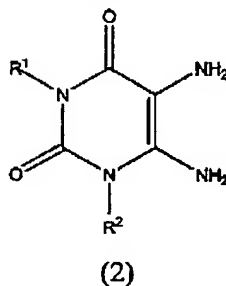


with a mixture of aqueous ammonia and sodium dithionite.

45. The process of claim 44, wherein the base is sodium ethoxide and the protic solvent is ethanol.

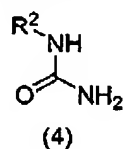
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46. The process of claim 6, wherein the compound of formula:



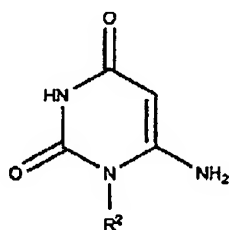
is prepared by a method comprising the steps of:

a) contacting a compound of the formula:



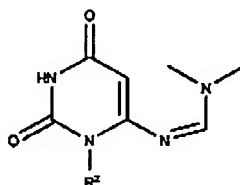
with ethyl cyanoacetate in the presence of a base in a protic solvent;

b) contacting the product thus formed:



with the dimethylacetal of N,N-dimethylformamide;

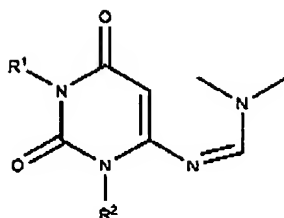
c) contacting the product thus formed:



with a compound of formula R¹L, in which L is a leaving group;

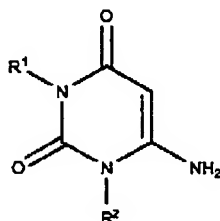
d) contacting the product thus formed:

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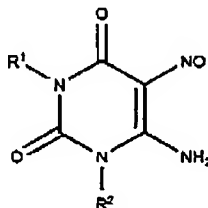
with aqueous ammonia;

e) contacting the product thus formed:



with a mixture of sodium nitrite in acetic acid/water; and

f) contacting the product thus formed:



with a mixture of aqueous ammonia and sodium dithionite.

47. The process of claim 46, wherein the base is sodium ethoxide and the protic solvent is ethanol.

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